Rejection under 35 U.S.C. §103(a)

Claims 1-22 remain rejected under 35 U.S.C. 103(a) as being unpatentable over the WO 97/12630 in view of Ragab U.S. 6,346,524 and Kline U.S. 6,180,096 or WO 95/13090. The Examiner maintains that motivation to combine the references comes from Kline and WO 95/13090.

In response, applicant provides the following comments. Applicant maintains its previous arguments that the prima facie case of obviousness has not been established in this case, that impermissible hindsight reconstruction has been applied to render these claims obvious and that the combination of references cited by the Examinerdo not contain the proper motivation to render the present invention obvious. Applicant maintains, for the reasons of record, and for the reasons below, that the obviousness rejection should be withdrawn.

As stated by the courts, motivation to combine references for an obviousness rejection cannot be derived from the applicant's specification. As per **Joy Technologies v. Flakt, Inc.**, 820 F. Supp. 802 (D. Del. 1993), the court held that the standard for obviousness is whether the prior art would have suggested to one of ordinary skill in the art that a process should be carried out and would have a reasonable likelihood of success, viewed in light of the prior art. Both the suggestion and the expectation of success must be founded in the prior art, and not in light of the applicant's disclosure (see also **In re Dow Chemical**, 837 F.2d 469 (Fed. Cir. 1988)). In **Grain Processing Corporation v. American Maize-Products**, 840 F.2d 902, 913 (Fed. Cir. 1988), the Federal Circuit stated that the question to ask to determine obviousness is whether there is something in the prior art as a whole to suggest the desirability, and thus the obviousness, of making the combination. Care must be taken to avoid hindsight reconstruction. **Id**. The obviousness inquiry is NOT whether each element existed in the prior art, but whether the prior art made obvious the invention as a whole for which patentability is claimed. **Id. at 14**. (see also generally, **Rosemount, Inc. v. Beckmann Instruments, Inc.**, 727 F.2d. 1540, 1546, 221 U.S.P.Q. 1, 7 (Fed. Cir. 1984)).

In **Uniroyal, Inc. v. Rudkin-Wiley Crop., 837 F.2d 1044, 1051, 5 U.S.P.Q.2d 1434, 1438** (Fed. Cir. 1988), the court held that when prior art references require selective combination by a court to render obvious a subsequent invention, there

must be some reason for the combination other than the hindsight gleaned form the invention itself. Something in the prior art as a whole must suggest the desirability, and thus the obviousness, of making the combination. **Id**. "Obvious to try" is not the standard under Section 103 by which obviousness is determined.

Applicant reiterates its previous arguments regarding the impermissibility of hindsight and obvious to try as standards for an obviousness rejection. Applicant notes that the Examiner has pointed out in the previous office actions where dosing regimens and parameters were shown in the cited art. However, the fact that these regimens and parameters exist in the cited art, does not necessarily mean there is an adequate basis for an obviousness rejection. As stated in **Rosemount, Inc. v. Beckmann Instruments, Inc.**, 727 F.2d. 1540, 1546, 221 U.S.P.Q. 1, 7 (Fed. Cir. 1984), a combination of prior art references may be patentable whether it be composed of elements all new, partly new, or all old. Applicant respectfully points out that it is NOT arguing these regimens and parameters for each component of the claimed invention are not found in the cited art. Rather applicant respectfully reiterates that none of the references **suggest or motivate** one of ordinary skill in the art to practice the claimed method of combination therapy with temozolomide and pegylated interferon. Applicant respectfully suggests that the claimed method has a synergistic advantage of utilizing this particular combination therapy at the claimed dosing levels and dosing schedule, to achieve higher response rates and/or reduced side effects in treating cancer patients. As support of this, applicant again refers the Examiner to the detailed clinical study design as described in the specification from pages 8 to 23.

Therefore, reconsideration and withdrawal of this ground of rejection is respectfully urged.

In view of the foregoing, applicant submits that the application, as pending, is in condition for allowance and courteously solicits a Notice of Allowance.

No fees, other than the payment of a Notice of Appeal, are believed to be due with this amendment. If any fees are determined to be due by this paper, the Commissioner is hereby authorized to deduct such fees from Account No. 19-0365.

The Examiner is requested to call the undersigned attorney on any matter connected with this application.

Respectfully submitted,

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